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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/270,983	03/17/99	HAY	B 06618/284001

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EXAMINER	
HUTSON,R	
ART UNIT	**PAPER NUMBER**
1652	8

DATE MAILED: 12/05/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/270,983	Hay et al
Examiner	**Group Art Unit**
Richard Hutson	1652

☒ Responsive to communication(s) filed on *Sep 19, 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-56* is/are pending in the applicat

Of the above, claim(s) *10-56* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-7 and 9* is/are rejected.

☒ Claim(s) *8* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claims 1-56 are still at issue and are present for examination.

Applicant's election of Group I, Claims 1-9 in Paper No. 7 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The requirement is deemed proper and is therefore made FINAL.

Claims 10-56 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Objections

1. Claim 8 is objected to because of the following informalities: Claim 8 is dependent on rejected claim 1. Appropriate correction is required.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 3-7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 (4-7 dependent on) is indefinite in the recitation of "nuclear export protein" as it is confusing as to the intended meaning of this phrase in light of knowledge possessed by one of skill in the art and the definition of "nuclear export protein" as defined at page 14, line 2 as a

polypeptide that directs the polypeptide to a region of a cell outside of the nucleus. While the definition may be interpreted as: 1) a polypeptide that directs the polypeptide to a region of a cell **other then the nucleus**, the definition may also be interpreted as 2) a polypeptide that directs the polypeptide from **a region inside the nucleus to a region outside of the nucleus** and given the meaning of the term "export" the later interpretation of the definition of "nuclear export protein" would be the plain meaning of this term. However, in view of the remainder of the specification, it appears that applicants intent was the first interpretation. It is suggested that this phrase be amended such that the interpretation is clearer.

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 3 (4-7 dependent on) is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As discussed above under 112 2nd paragraph rejection, claim 3 recites the fusion protein of claim 1, wherein said repressor polypeptide comprises a nuclear export sequence that directs the localization of said fusion protein outside of the nucleus of a cell. While the specification defines at page 14, line 2 that a "nuclear export sequence" is a polypeptide that directs the polypeptide to a region of a cell outside of the nucleus, the specification fails to describe a

polypeptide that directs the localization of said polypeptide outside of the nucleus of a cell (See discussion above of interpretation of "nuclear export protein"). One of skill in the art would consider such a protein sequence to direct the localization of said protein from inside the nucleus to outside of the nucleus. The specification describes a number of "signal peptides" or peptides that act as localization sequences including those that target the nucleus, mitochondrion, endoplasmic reticulum, peroxisome, golgi apparatus and the plasma membrane (page 14, line 13 thru page 15, line 5). None of the described localization sequences or the "nuclear export sequences" have been shown to direct the localization of said polypeptide from inside the nucleus to outside of the nucleus nor is there any evidence that such sequences are known in the art. One of ordinary skill in the art would not be able to make the fusion protein of claim 3, drawn to the fusion protein of claim 1, wherein said repressor polypeptide comprises a nuclear export sequence that directs the localization of said fusion protein outside of the nucleus of a cell.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention drawn to the fusion protein of claim 1, wherein said repressor polypeptide comprises a nuclear export sequence that directs the localization of said fusion protein outside of the nucleus of a cell. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of substances having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

7. Claims 1, 2, 3 and 9 are rejected under 35 U.S.C. 102(e) as being anticipated by Tsien et al. (U.S. Patent No. 5,981,200).

Tsien et al. teach constructs of tandem fluorescent proteins constructs including a donor moiety, an acceptor moiety and a linker moiety that couples the donor and acceptor moieties. Fluorescent proteins are known cytoplasmic proteins. The donor and acceptor moieties exhibit fluorescence energy transfer which is eliminated upon cleavage of the linker moiety. Further, Tsien et al. teach the use of said protein constructs in assays to determine whether a compound alters the activity of an enzyme, i.e., screening assays. Tsien et al. teach that the linker can comprise a peptide containing a cleavage recognition sequence for a specific protease and lists a number of particular cleavage sequences for a number of different proteases, including interleukin-1b-converting enzyme (Caspase-1)(Table II).

Therefore, Tsien et al. anticipates claims 1, 2, 3 and 9.

8. Claims 1, 3 and 9 are rejected under 35 U.S.C. 102(b) as being anticipated by Knight. (Methods in Enzymology 248: 18-34, 1995).

Knight et al. teach constructs of fluorescent proteins comprising an appropriate peptide sequence (linker) which separates a fluorophore from another group that quenches the fluorescence via intramolecular contacts (page 19, first paragraph). Knight also teach related molecules which employ the principle of resonance energy transfer, by which the fluorescent donor can be efficiently quenched by a suitable acceptor even when the groups are separated by 10 or more residues. Further, Knight teach the use of said protein constructs in assays to determine the protease activity.

Therefore, Knight anticipates claims 1, 3 and 9.

Of interest are Dasmahapatra (U.S. Patent No. 5,599,906) and Germann et al. (U.S. Patent No. 6,117,639) drawn to protein constructs and methods of their use in protease assays.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on M-F from 7:30 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapy Achutamurthy (Murthy), can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard Hutson Ph.D.
11/29/2000

Rebecca Prouty

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